

Figure 1

1. Generate Ensemble

20,000 conformational states

2. Calculate Gibbs Energy

20,000 ΔG values

3. Identify ΔG s of Binding Competent States

"a" bc ΔG s "20,000-a" non-bc ΔG s

4. Modify bc ΔG s

"a" bc ΔG^* s

5. Form two sets of ΔG values, with and w/o ligand. Compute probabilities

20,000 ΔG s + ligand
bc ΔG^* s non-bc ΔG s

20,000 ΔG s - ligand
bc ΔG s non-bc ΔG s

6. Calculate stability Constants

20,000 P_s + ligand
bc P_s^* non-bc P_s

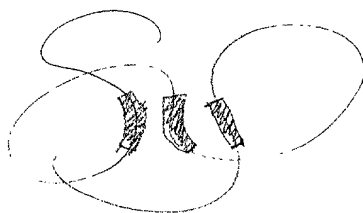
20,000 P_s - ligand
bc P_s non-bc P_s

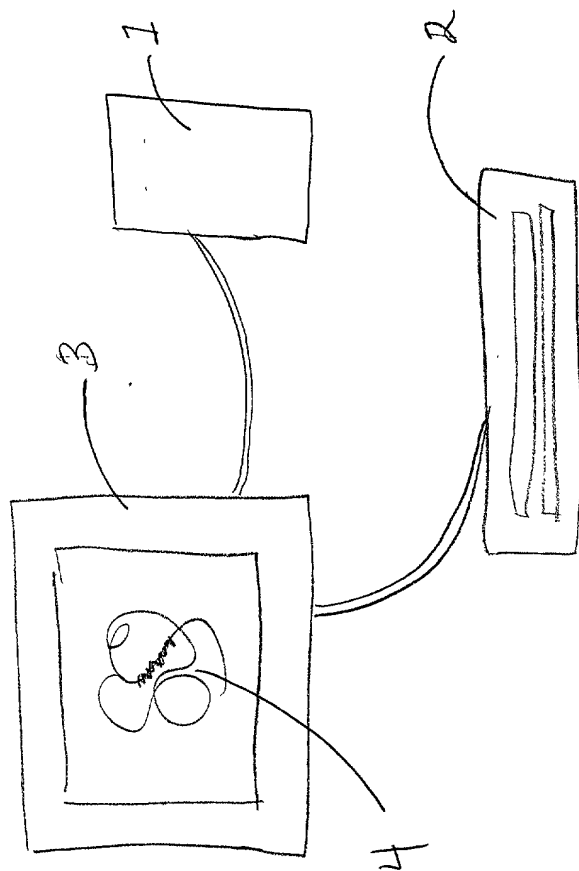
7. Compare K values and select affected residues

n K + ligand
 K_s

n K - ligand
 K_s

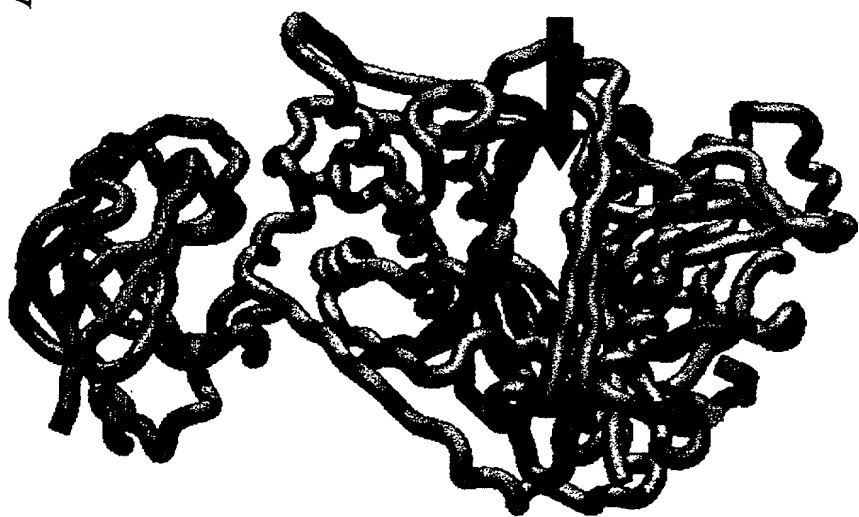
8. Create and display model.





102600 400500

A



B



C

